IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Y.V.S.N. MURTHY	Confirmation No.: 4452
Application No.: 10/623,114	Group Art Unit: 1617
Filed: July 18, 2003	Examiner: J. Kim
For: COMPOSITIONS CONTAINING PRODRUGS OF FLORFENICOL	Attorney Docket No.: 13390-07011

DECLARATION UNDER 37 C.F.R. § 1.132

U.S. Patent and Trademark Office
Customer Service Window
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Alexandria, VA 22314

Sir:

I Yerramilli V.S.N. Murthy, the inventor on the above-identified U.S. patent application, *i.e.*, U.S. patent application serial no. 10/623,114 ("the '114 application"), hereby declare that:

1. I am a citizen of the United States and I reside at 2212 Oak Stream Lane, Apex North Caroline, 27523.

2. I am a research manager for IDEXX laboratories Inc. I have a Ph.D. in chemistry and have been involved in chemical research for over 15 years. I am an inventor on over 20 U.S. patents or patent applications.

3. Under my direction and supervision a study was conducted to compare the toxicity of sub-cutaneously administered florfenicol (Nufluor® commercially available from Schering-Plough Corp. of Kenilworth, NJ) and sub-cutaneously administered florfenicol butyrate.

4. The florfenicol butyrate composition ("the florfenicol butyrate composition") was prepared by the following general procedure :weigh about 70 g of florfenicol butyrate into a 200 mL volumetric flask, add about 20 mL of propylene glycol, fill the flask to a volume of about 100 mL with glycerol formal to provide a suspension, sonicate the suspension for about 15 minutes followed by shaking for about 1 hour on a shaker, add more glycerol formal to provide a volume of about 150 mL, shake the resulting mixture until a clear solution is obtained, fill the flask to 200 mL with glycerol formal, and mix it well to provide a homogenous solution.

5. On Day 0, two cats (1 male and 1 female) were each administered florfenicol as a subcutaneous injection of Nuflor® at a dose of 120 mg/kg and two cats (1 male and 1 female) were each administered florfenicol butyrate as a subcutaneous injection of the florfenicol

butyrate composition at a dose of 120 mg/kg. Each animal was observed for 40 days post dose for injection site reactions and other abnormalities. The following observation were made:

- $ On Day 6, the female cat administered NuFlor® had a large swelling / lump at the injection site. No swelling was observed for the female injected with the florfenicol butyrate composition.

- $ On Day 10, the male cat administered NuFlor® vomited a greenish/yellow liquid indicating possible hepatotoxicity.

- $ On Day 11, the male cat administered NuFlor® did not eat, excreted no feces, and vomited approximately 3-5 ml of a greenish/yellow liquid.

- $ On Day 12, the male cat administered NuFlor® did not eat, excreted no feces, vomited approximately 3-5 ml of a greenish/yellow liquid, and had pupils that appeared dialated. The injection site of the female cat administered NuFlor® still felt warm.

- $ On Day 13, the male cat administered NuFlor® still did not eat and excreted no feces.

6. The results of these experiments demonstrate that administering Nuflor® (*i.e.*, florfenicol) to cats by subcutaneous injection at a dose of 120 mg/kg has serious adverse effects. In contrast, administering florfenicol butyrate to cats by subcutaneous injection at a dose of 120 mg/kg results in fewer and less severe adverse effects. As demonstrated by Example 8 and FIG. 8 of the '114 application, administration of florfenicol butyrate has a better pharmacological profile than administration of florfenicol. In particular, administration of florfenicol butyrate provides a lower C_{max} for florfenicol and higher serum concentrations of florfenicol for a longer period of time, *i.e.*, a greater AUC. Thus, administering florfenicol butyrate to cats advantageously provides higher serum concentrations of florfenicol, compared to administering florfenicol, yet, as described above, is also less toxic.

7. I further declare that all statements made herein of my knowledge are true and all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Dated this 19 day of JAN, 2007

Yerramilli V.S.N. Murthy, Ph.D.